REMARKS

This is a full and timely response to the final Office Action mailed October 6, 2008. Reconsideration of the application and allowance of presently pending claims as amended, are respectfully requested.

A. Present Status of Patent Application

Claim 99 is amended herein solely to change dependency. New claims 100 and 101 are added. Support for new claims 100 and 101 is found at least at paragraph 0032 and Fig 1 of applicants' specification.

Claims 1-15, 18-20, 23-25, 28-31, 38-40, 63-78 and 98-101 remain pending.

B. Response to Rejections

1. Claim Objections

Claim 99 was objected to as an improper dependant claim. This claim now depends from claim 63.

2. Provisional Double Patenting Rejection

Claims 1-15, 18-20, 23-25, 28-31, 38-40, 98 and 99 were rejected on the ground of nonstatutory obviousness-type double patenting over the claims of co-pending U.S. application 11/187,757 in view of Straub et al and further in view of Schmitt et al. Should this provisional rejection mature into a double-patenting rejection which is the sole ground of rejecting the present claims, consideration will be given to filing the appropriate terminal disclaimer.

3. Rejection under 35 U.S.C. §103(a) over *Ponikau.*

Claims, 1-15, 18-20, 23-25, 28-31, 38-40, 63-76, 98 and 99 were rejected under 35 USC 103(a) as allegedly unpatentable over *Ponikau*, US 6207703, in view of *Straub et al.*, US 6395300.

Applicants again traverse this rejection for at least the following reasons.
Neither reference, individually, or in combination teaches the subject matter of the cited claims. Moreover, as further described herein, it is **improper to combine** the two references.

Applicant's Independent claims each require *inter alia*, an aerosolized porous powder characterized by a mass median aerodynamic diameter (MMAD) of less than about 5 microns, and administration sufficient to achieve a 2x MIC lung concentration for at least about one week.

Neither reference contemplates, teaches or suggests delivering powders to the lungs to treat infections thereof, and therefore, neither reference can possibly disclose, teach or suggest the claimed particle properties, such as MMAD, which allow for such lung deliver and concomitant efficacy in the lung.

As stated in a prior response, *Ponikau* is limited to teaching methods and materials for treating a non-invasive fungus-induced rhinosinusitis, and has nothing to do with pulmonary fungus or pulmonary delivery and in particular does not teach or suggest methods and formulations comprising powders for pulmonary delivery. As such *Ponikau* does not teach or suggest the elements of applicants' amended claims, in particular the features of **porous, aerodynamically light** powders, having the claimed bulk density and mass median aerodynamic diameter characteristics for delivery to the lungs to treat infections of the lungs.

Ponikau is limited to teaching mucoadministration for rhinosinusitis. This is far removed from applicants' claimed invention comprising lung delivery for lung infections. The bare fact that *Ponikau* states that the formulation thereof can be a powder does not constitute a

teaching that such a powder is capable or suitable for pulmonary delivery (indeed, it cannot be, since *Ponikau* is limited to infections of the upper respiratory tract).

Straub et al. is inapposite because *Straub et al.* is drawn to a method of improving rate of dissolution of orally or parenterally-administered drugs, especially those with low aqueous solubilities. Straub thus does not teach suggest or disclose anything relating to aerodynamically-light particles for **pulmonary administration** directly to the lung, and in particular does not teach suggest or disclose a particulate formulation having the properties as claimed and wherein the formulation is administered by the claimed method to treat pulmonary fungal infections

It was contended that *Straub et al*, at column 3 line, teaches dry powder administration. Applicant responds that dry powder administration of certain drugs is well known. What is not taught or suggested by the art, including *Straub et al.*(notwithstanding this unsupported statement) are one of more claimed elements of the requisite aerodynamic properties of a powder to afford therapeutic effect of a drug delivered in this manner; nor specific drug formulations, nor the target concentrations achieved, to name a few. This statement in *Straub et al* is wholly unsupported, and as such, does not rise to the level of a teaching such that applicants claims are rendered unpatentable.
While it was contended in the Action that *Straub et al* teaches pulmonary administration as a preferred embodiment, in fact a review of *Straub et al.* affirmatively discloses that the **preferred embodiment is liquid, intramuscular, subcutaneously or intravenously**:

> **In a preferred embodiment, the porous drug matrix is reconstituted with an aqueous medium and administered- parenterally, such as intramuscularly, isubcutaneously, or intravenously.** Alternatively, the porous drug matrix can be further processed using standard techniques into tablets or capsules for oral administration or into rectal suppositories, delivered using a dry powder inhaler for pulmonary administration, or mixed/processed into a cream or ointment for topical administration. [emphasis added]

Straub et al., Column 3, lines 1-9

There is thus insufficient motivation in *Straub et al.* to teach one skilled in the art to make a powder pharmaceutical formulation **for aerosolization** comprising an antifungal

agent having efficacy against pulmonary fungal growth, wherein the powder comprises porous particles, and is characterized by a mass median aerodynamic diameter of less than about 5 microns and a bulk density of less than about 0.5 g/cm^3, the powder formulation being administered in a first and a second dosage, said first dosage being greater than said second dosage, wherein a sufficient amount of the pharmaceutical formulation is administered to maintain for at least one week a target antifungal agent lung concentration of at least two times the determined minimum inhibitory concentration.

Moreover, a review of the disclosure of *Straub et al.* makes it clear that engineering particles for inhalation purposes is **not** a feature the alleged invention therein. *Straub et al.* is specific in making a particle which **enhances a rate of drug dissolution and either stabilizes the drug in crystalline form or in amorphous form.**

> This invention generally relates to formulations of drugs, especially drugs having low solubility, and more particularly to methods of making formulations of such drugs to enhance their rate of dissolution.
>
> The bioavailability of a drug can be limited by poor dissolution of the drug into aqueous bodily fluids following administration. This rate-limiting step may therefore be critical to rapidly attaining therapeutically effective drug levels.

Straub et al., paragraph 0002

An invention directed at improving dissolution is not the same as that relating to a particle engineered for delivery of an antifungal agent to the situs of an infection in the lung for effecious treatment thereof.

As such, there is further no motivation or suggestion to combine *Straub et al.* with *Ponikau,* as the two relate to entirely different routes of administration and purposes. Even if there were such a teaching, the result would still not result in applicants' claimed invention, since neither reference relates to particles engineered for pulmonary administration, and methods of treatment therewith.

4. Claims 77 and 78 were rejected under 35 USC 103(a) as allegedly unpatentable over *Ponikau*, US 6207703, in view of *Straub et al.*, US 6395300, and further in view of *Gomez et al.* US 5854280.

Applicants respectfully traverse the rejection of these dependent claims for the same reasons advanced in paragraph 3 above. The combination of *Ponikau, and/or Straub et al.* and/or *Gomez et al.* (which applicants contend is improper in any event) does not change this conclusion.

Gomez et al. relates specifically to a novel sordaridin antifungal compound, and not to a method of treating or providing therapy against fungal infections wherein the method comprises administering by inhalation a dry powder having one of more claimed elements of the requisite aerodynamic properties of a powder to afford therapeutic effect of a drug delivered in this manner; nor specific drug formulations, nor the target concentrations achieved, to name a few. While *Gomez et al.* discloses dry powder delivery (column 8, lines 56-64), there is no teaching of how to do so in an efficacious manner. *Gomez et al.* simply recites inhalation delivery as a possibility, along with the all other possibly conceivable routes of administration. *Gomez et al.*, either alone, or combined with *Ponikau and/or Strau et al.*, does not teach, suggest or disclose applicants specifically claimed method of treating and/or preventing pulmonary infections, including administering in the claimed dosage and regimen.

Additionally, as to any rejection made in the Action of any dependent claims, as the independent claims are contended to be allowable over the prior art of record, then their dependent claims are allowable as a matter of law, because these dependent claims contain all features/elements/steps of their respective independent claim. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). Additionally and notwithstanding the foregoing reasons for the allowability of independent claims 1, 23 and 63 the dependent claims recite further features/steps and/or combinations of features/steps (as is apparent by examination of the claims themselves) that are patentably distinct from the prior art of record. Hence, there are other reasons why these dependent claims are allowable.

Conclusion

In view of the foregoing, applicants submit that pending claims 1-15, 18-20, 23-25, 28-31, 38-40, 63-78 and 98-101, satisfy the requirements of patentability and are therefore in condition for allowance. Reconsideration and withdrawal of all rejections is respectfully requested and a prompt mailing of a Notice of Allowance is solicited.

Please grant any extensions of time required to enter this response and charge any additional required fees to deposit account .

If a telephone conference would expedite the prosecution of the subject application, the Examiner is requested to call the undersigned at (650) 283-6790.

Respectfully submitted,

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